In the Claims

Applicants present replacement claims below indicating the changes with insertions indicated by underlining and deletions indicated by strikeouts.

1. (Currently Amended) ~~A~~ The method ~~for determining the presence of at least one analyte, comprising~~ of claim 188, wherein the act of identifying each of the one or more nucleotides comprises:

providing a sample comprising a plurality of aggregates of size of at least about 500 nm;

adsorbing ~~a plurality of analytes~~ at least some of the one or more nucleotides to at least some of the plurality of aggregates;

exposing the sample to electromagnetic radiation to cause surface-enhanced emission;

obtaining spectral information of the sample, wherein at least one spectral line of the information represents a single ~~analyte~~ nucleotide adsorbed on one of the plurality of aggregates; and

determining the presence of the single ~~analyte~~ nucleotide from the at least one spectral line.

2. (Currently Amended) A method as in claim 1, the exposing step ~~involving~~ comprising exposing the sample to electromagnetic radiation and causing Raman scattering of the sample, and the obtaining step comprising obtaining Raman information of the sample, wherein a single Raman line of the information represents the single ~~analyte~~ nucleotide.

3. (Original) A method as in claim 1, wherein the sample is free of an emission-enhancing aid.

4. (Original) A method as in claim 1, wherein the spectral information is a surface-enhanced Raman spectrum, having an enhancement factor of at least about 10^{10}.

5. (Original) A method as in claim 1, wherein each aggregate of the plurality of aggregates comprises a plurality of metal particles.

6. (Currently Amended) A method as in claim 5, wherein ~~the plurality~~ at least some of the metal particles ~~is~~ are selected from the group consisting of silver, gold and copper particles.

7. (Currently Amended) A method as in claim 6, wherein the plurality of aggregates is formed in situ by exposure to the electromagnetic radiation.

8. (Original) A method as in claim 1, wherein the plurality of aggregates is selected from the group consisting of colloids suspended in a medium, aggregates deposited on a substrate and lithography-produced metal aggregates.

9. (Original) A method as in claim 8, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

10. (Original) A method as in claim 8, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.

11. (Original) A method as in claim 1, wherein the sample consists essentially of a plurality of aggregates of from about 500 nm to about 20 microns in dimension.

12. (Original) A method as in claim 1, wherein the electromagnetic radiation is non-resonant radiation.

13. (Original) A method as in claim 12, wherein the electromagnetic radiation is near infrared radiation.

14. (Original) A method as in claim 1, wherein the spectral information is Raman information that defines less than a complete Raman spectrum.

15. (Original) A method as in claim 14, wherein the spectral information is less than 5 Raman lines.

16. (Original) A method as in claim 14, wherein the spectral information is less than 2 Raman lines.

17. (Original) A method as in claim 1, wherein the spectral information is a single Raman line.

18. (Cancelled)

19. (Currently Amended) A method as in claim 1, wherein the single ~~analyte~~ nucleotide is selected from the group consisting of thymine, adenine, cytosine, guanine, and uracil.

20-22. (Cancelled)

23. (Currently Amended) ~~A~~ The method ~~for determining the presence of an analyte, comprising~~ of claim 188, wherein the act of identifying each of the one or more nucleotides comprises:

providing a sample comprising a plurality of aggregates;

adsorbing ~~a plurality of analytes~~ each of the one or more nucleotides to at least some of the plurality of aggregates, wherein at least one aggregate of the plurality of aggregates comprises a metal cluster of at least seven particles and adsorbs only one ~~analyte~~ nucleotide;

exposing the sample to electromagnetic radiation to cause surface-enhanced emission;

obtaining spectral information of the sample, wherein the only one ~~analyte~~

nucleotide contributes to the spectral information; and

determining the presence of the only one ~~analyte~~ nucleotide from the spectral information.

24. (Currently Amended) A method as in claim 23, the exposing step ~~involving~~ comprising exposing the sample to electromagnetic radiation to cause Raman scattering, and the obtaining step ~~involves~~ comprises obtaining a Raman spectrum of the sample, wherein the only one ~~analyte~~ nucleotide contributes to at least one Raman signal of the Raman spectrum.

25. (Original) A method as in claim 23, wherein the plurality of aggregates comprises a metal cluster of at least ten particles.

26. (Original) A method as in claim 23, wherein the plurality of aggregates comprises a metal cluster of at least twenty particles.

27. (Original) A method as in claim 23, wherein the plurality of aggregates comprises a metal cluster of at least thirty-five particles.

28. (Original) A method as in claim 23, wherein the sample is free of an emission-enhancing aid.

29. (Currently Amended) A method as in claim ~~23~~ 24, wherein the Raman spectrum is a surface-enhanced Raman spectrum, having an enhancement factor of at least ~~1010~~ 10^{10}.

30. (Currently Amended) A method as in claim 23, wherein the metal cluster of at least seven particles ~~are~~ comprises particles selected from the group consisting of silver, gold and copper particles.

31. (Currently Amended) A method as in claim 23, wherein the plurality of aggregates is formed in situ by exposure to the electromagnetic radiation.

32. (Original) A method as in claim 23, wherein the plurality of aggregates is selected from the group consisting of a colloids suspended in a medium, aggregates deposited on a substrate and lithography produced metal aggregates.

33. (Original) A method as in claim 32, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

34. (Original) A method as in claim 32, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.

35. (Currently Amended) A method as in claim 23, wherein at least some of the ~~at least one~~ aggregates ~~has~~ have a dimension of at least about 500 nm.

36. (Original) A method as in claim 23, wherein the electromagnetic radiation is non-resonant radiation.

37. (Original) A method as in claim 36, wherein the electromagnetic radiation is near infrared radiation.

38. (Cancelled)

39. (Currently Amended) A method as in claim 23, wherein the ~~single analyte~~ only one nucleotide is selected from the group consisting of thymine, adenine, cytosine, guanine, and uracil.

40-42. (Cancelled)

43. (Original) A method as in claim 23, wherein the sample consists essentially of aggregates of size of from about 500 nm to about 20 microns.

44. (Currently Amended) A method as in claim 23, wherein the ~~at least one~~ plurality of aggregates comprises a plurality of metal particles each having a dimension of no more than about 100 nm.

45. (Currently Amended) A method as in claim 23, wherein the ~~at least one~~ plurality of aggregates comprises a plurality of metal particles each having a dimension of no more than about 75 nm.

46. (Currently Amended) ~~A~~ The method ~~for determining the presence of an analyte, comprising~~ of claim 188, wherein the act of identifying each of the one or more nucleotides comprises:

providing a sample comprising a plurality of aggregates;

adsorbing ~~a plurality of analytes~~ at least some of the one or more nucleotides to at least some of the plurality of aggregates, wherein each aggregate comprises a plurality of metal particles, each metal particle having a dimension of no more than about 100 nm and at least one aggregate adsorbs only one ~~analyte~~ nucleotide;

exposing the sample to electromagnetic radiation to cause surface-enhanced emission;

obtaining spectral information of the sample, wherein the only one ~~analyte~~ nucleotide contributes to the spectral information; and

determining the presence of the only one ~~analyte~~ nucleotide from the spectral information.

47. (Currently Amended) A method as in claim 46, wherein the exposing step ~~involves~~ comprises causing surface-enhanced emission and the obtaining step ~~involves~~ comprises obtaining Raman spectral information.

48. (Original) A method as in claim 46, wherein the sample is free of an emission-enhancing aid.

49. (Currently Amended) A method as in claim 46, wherein the spectral information is a surface-enhanced Raman spectrum, having an enhancement factor of at least ~~1010~~ 10^{10}.

50. (Currently Amended) A method as in claim 46, wherein at least some of the metal particles are selected from the group consisting of silver, gold and copper particles.

51. (Currently Amended) A method as in claim 46, wherein the plurality of aggregates is formed in situ by exposure to the electromagnetic radiation.

52. (Original) A method as in claim 46, wherein the plurality of aggregates is selected from the group consisting of a colloids suspended in a medium, aggregates deposited on a substrate and lithography produced metal aggregates.

53. (Original) A method as in claim 52, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

54. (Original) A method as in claim 52, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.

55. (Original) A method as in claim 46, each metal particle having a dimension of no more than about 75 nm.

56. (Original) A method as in claim 46, wherein the electromagnetic radiation is non-resonant radiation.

57. (Original) A method as in claim 56, wherein the electromagnetic radiation is near infrared radiation.

58. (Original) A method as in claim 46, wherein the spectral information consists essentially of less than 5 lines of a Raman spectrum.

59. (Cancelled)

60. (Currently Amended) A method as in claim 46, wherein the ~~single analyte~~ only one nucleotide is selected from the group consisting of thymine, adenine, cytosine, guanine, and uracil.

61-63. (Cancelled)

64. (Currently Amended) ~~A~~ The method ~~for determining the presence of at least one analyte, comprising~~ of claim 188, wherein the act of identifying each of the one or more nucleotides comprises:

providing a sample comprising a plurality of aggregates~~,~~;

to at least one aggregate, adsorbing only one ~~analyte~~ nucleotide that is free of an emission-enhancing aid;

exposing the sample to electromagnetic radiation; and

obtaining a spectrum, wherein the only one ~~analyte~~ nucleotide contributes to at least one signal of the spectrum.

65. (Currently Amended) A method as in claim 64, wherein the spectrum is a surface-enhanced Raman spectrum, having an enhancement factor of at least ~~1010~~ 10^{10}.

66. (Original) A method as in claim 64, wherein each aggregate of the plurality of aggregates comprises a plurality of metal particles.

67. (Currently Amended) A method as in claim 66, wherein at least some of the metal particles are selected from the group consisting of silver, gold and copper particles.

68. (Original) A method as in claim 64, wherein the plurality of aggregates is formed in situ by exposure to the electromagnetic radiation.

69. (Original) A method as in claim 64, wherein the plurality of aggregates is selected from the group consisting of a colloids suspended in a medium, aggregates deposited on a substrate and lithography produced metal aggregates.

70. (Original) A method as in claim 69, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

71. (Original) A method as in claim 69, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.

72. (Currently Amended) A method as in claim 64, wherein at least some of the ~~at least one~~ aggregates ~~has~~ have a dimension of at least about 500 nm.

73. (Cancelled)

74. (Currently Amended) A method as in claim 64, wherein the ~~single analyte~~ only one nucleotide is selected from the group consisting of thymine, adenine, cytosine, guanine, and uracil.

75-77. (Cancelled)

78. (Currently Amended) ~~A~~ The method ~~for determining the presence of a single analyte, comprising~~ of claim 188, wherein the act of identifying each of the one or more nucleotides comprises:

providing a sample comprising a plurality of surfaces~~,~~;

to a portion of the plurality of surfaces, adsorbing only one ~~analyte~~ nucleotide;

and

exposing the sample to electromagnetic radiation to cause the sample to emit radiation such that the sample is free of photobleaching.

79. (Original) A method as in claim 78, wherein the plurality of surfaces comprises a plurality of aggregates.

80. (Original) A method as in claim 79, wherein the plurality of aggregates comprises a plurality of metal particles.

81. (Currently Amended) A method as in claim 80, wherein at least some of the metal particles are selected from the group consisting of silver, gold and copper particles.

82. (Original) A method as in claim 79, wherein the plurality of aggregates is selected from the group consisting of a colloids suspended in a medium, aggregates deposited on a substrate and lithography produced metal aggregates.

83. (Original) A method as in claim 82, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

84. (Original) A method as in claim 82, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.

85. (Original) A method as in claim 78, wherein the plurality of surfaces comprises a plurality of aggregates of metal particles, each of the metal particles having a dimension of no more than about 100 nm.

86. (Cancelled)

87. (Currently Amended) A method as in claim 78, wherein the only one ~~analyte~~ nucleotide is selected from the group consisting of thymine, adenine, cytosine, guanine, and uracil.

88-90. (Cancelled)

91. (Currently Amended) ~~A~~ The method ~~for determining the presence of at least one molecule, comprising~~ of claim 188, wherein the act of identifying each of the one or more nucleotides comprises ~~providing at least one molecule,~~ exposing ~~the at least one molecule~~ each of the one or more nucleotides to electromagnetic radiation to cause Raman scattering, obtaining Raman spectral information, and determining the presence of ~~the at least one molecule~~ each of the one or more nucleotides from at least one anti-Stokes line.

92. (Currently Amended) A method as in claim 91, wherein ~~the at least one molecule~~ each of the one or more nucleotides is adsorbed on a plurality of surfaces.

93. (Currently Amended) A method as in claim 91, wherein ~~the~~ at least one ~~analyte~~ nucleotide is exposed to non-resonant radiation.

94. (Currently Amended) A method as in claim ~~92~~ 91, wherein the electromagnetic radiation is near infrared radiation.

95. (Original) A method as in claim 94, wherein the near infrared radiation has a wavelength of at least 1000 nm.

96. (Currently Amended) ~~A~~ The method ~~for sequencing at least a portion of DNA or RNA, comprising~~ of claim 188, wherein the act of identifying each of the one or more nucleotides comprises:

~~cleaving the at least a portion of DNA or RNA into DNA or RNA fragments, wherein each fragment comprises at least one base;~~

allowing each ~~DNA or RNA fragment~~ of the one or more nucleotides to become surface-adsorbed;

exposing each ~~fragment~~ of the one or more nucleotides to electromagnetic radiation to cause surface-enhanced emission; and

obtaining unique surface-enhanced spectral information attributed to each ~~fragment~~ of the one or more nucleotides.

97. (Currently Amended) A method as in claim 96, wherein each ~~fragment~~ of the one or more nucleotides is surface-adsorbed onto one of a plurality of surfaces.

98. (Original) A method as in claim 97, wherein the plurality of surfaces is included in a moving stream.

99. (Currently Amended) A method as in claim 97, wherein the ~~plurality of~~ surfaces ~~is~~ are surfaces of aggregates, the aggregates being selected from the group consisting of a plurality of aggregates suspended in a medium, a plurality of aggregates deposited on a substrate and lithography produced metal aggregates.

100. (Original) A method as in claim 99, wherein the plurality of aggregates comprise clusters of metal particles.

101. (Currently Amended) A method as in claim 100, wherein at least some of the metal particles are selected from the group consisting of silver, gold and copper particles.

102. (Original) A method as in claim 99, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

103. (Original) A method as in claim 100, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.

104. (Original) A method as in claim 96, comprising allowing each ~~fragment~~ of the one or more nucleotides to become surface-absorbed on a plurality of protrusions and voids on a rough metal film.

105. (Original) A method as in claim 96, wherein the electromagnetic radiation is non-resonant radiation.

106. (Original) A method as in claim 96, wherein the electromagnetic radiation is near infrared radiation.

107. (Currently Amended) ~~A~~ The method ~~for general field enhancement, comprising~~ of claim 188, wherein the act of identifying each of the one or more nucleotides comprises providing a plurality of aggregates, attaching each of the one or more nucleotides to one or more aggregates, exposing the plurality of aggregates to near infrared radiation, and inducing at least one electromagnetic resonance in the plurality of aggregates to cause a surface-enhanced radiation.

108. (Original) A method as in claim 107, wherein the near infrared radiation has a wavelength of at least 1000 nm.

109. (Original) A method as in claim 107, wherein the plurality of aggregates comprises a plurality of metal particles.

110. (Original) A method as in claim 109, wherein at least some of the metal particles are selected from the group consisting of silver, gold and copper particles.

111. (Currently Amended) A method as in claim 107, wherein the plurality of aggregates is formed in situ by exposure to the electromagnetic radiation.

112. (Original) A method as in claim 107, wherein the plurality of aggregates is selected from the group consisting of colloids suspended in a medium, aggregates deposited on a substrate and lithography produced metal aggregates.

113. (Original) A method as in claim 112, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

114. (Original) A method as in claim 112, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.

115. (Original) A method as in claim 109, wherein each metal particle has a dimension of no more than about 100 nm.

116. (Original) A method as in claim 109, wherein the plurality of aggregates comprises at least seven metal particles.

117. (Currently Amended) A method as in claim 107, wherein the surface enhanced radiation has an enhancement factor of at least ~~1010~~ 10^{10}.

118-121. (Cancelled)

122. (Currently Amended) ~~A~~ The method ~~for determining the presence of an analyte, comprising~~ of claim 188, wherein the act of identifying each of the one or more nucleotides comprises:

providing a sample comprising a rough metal film including a plurality of protrusions and indentations;

absorbing ~~a plurality of analytes~~ the one or more nucleotides on a surface of the film;

exposing the sample to electromagnetic radiation to cause Raman scattering; and

obtaining a unique Raman signal attributed to a single ~~analyte~~ nucleotide.

123-124. (Cancelled)

125. (Currently Amended) ~~A~~ The method of claim 188, comprising:

~~a)~~ sequentially removing the one or more nucleotides from one end of ~~at least one~~ the nucleic acid~~;~~

~~b) attaching each nucleotide to at least one nanoparticle;~~

~~c) identifying said nucleotides; and~~

~~d) determining the sequence of said nucleic acid~~.

126. (Currently Amended) The method of claim ~~125~~ 188, wherein said nucleic acid is attached to a surface.

127. (Cancelled)

128. (Currently Amended) The method of claim ~~125~~ 188, wherein said nucleotides are identified by surface enhanced Raman spectroscopy (SERS) and/or surface enhanced resonance Raman spectroscopy (SERRS).

129. (Cancelled)

130. (Currently Amended) The method of claim ~~129~~ 188, wherein each nucleotide is attached to a single nanoparticle or a nanoparticle aggregate.

131. (Cancelled)

132. (Previously Presented) The method of claim 128, further comprising exciting said nucleotides with a laser.

133. (Previously Presented) The method of claim 132, wherein a charge coupled device (CCD) camera is used to identify said nucleotides.

134. (Currently Amended) The method of claim ~~125~~ 188, further comprising recording the identity of each nucleotide and the time at which each nucleotide is identified.

135. (Currently Amended) The method of claim ~~125~~ 188, wherein an exonuclease is used to remove said nucleotides from said nucleic acid.

136-137. (Cancelled)

138. (Currently Amended) ~~A~~ The method of claim 188, further comprising, prior to the act of removing one or more nucleotides from the nucleic acid:

~~a)~~ obtaining one or more nucleotides that are attached to Raman labels; and

~~b)~~ providing a nucleic acid comprising the labeled nucleotides~~;~~

~~c) removing nucleotides from one end of the nucleic acid;~~

~~d) identifying nucleotides by Raman spectroscopy; and~~

~~e) determining the sequence of the nucleic acid~~.

139. (Currently Amended) The method of claim ~~138~~ 188, further comprising passing the nucleotides removed from the nucleic acid in a stream.

140-145. (Cancelled)

146. (Currently Amended) The method of claim ~~138~~ 188, wherein said nucleotides are removed from said nucleic acid by exonuclease activity.

147. (Previously Presented) The method of claim 146, wherein only one nucleic acid at a time is exposed to exonuclease activity.

148-152. (Cancelled)

153. (Currently Amended) ~~A~~ The method of claim 188, comprising:

~~a) sequentially removing nucleotides from one end of at least one nucleic acid;~~

~~b)~~ moving the nucleotides in a stream packed with nanoparticles~~;~~

~~c) identifying the nucleotides by Raman spectroscopy; and~~

~~d) determining the sequence of the nucleic acid~~.

154. (Cancelled)

155. (Currently Amended) The method of claim ~~153~~ 188, further comprising attaching said nucleic acid to a surface.

156. (Currently Amended) The method of claim ~~155~~ 188, wherein said nucleic acid is immobilized in a reaction site.

157. (Previously Presented) The method of claim 156, wherein a single nucleic acid is immobilized in said reaction site.

158. (Cancelled)

159. (Previously Presented) The method of claim 153, wherein at least two nanoparticles are cross-linked together.

160. (Previously Presented) The method of claim 153, wherein the nanoparticles comprise gold and/or silver, said nanoparticles between about 10 nm and 20 micrometers in size.

161. (Previously Presented) The method of claim 160, wherein the size of said nanoparticles is selected from the group consisting of about 10 to 50 nm, about 10 to 100 nm, about 10 nm and about 500 nm.

162. (Currently Amended) ~~A~~ The method of claim 188, further comprising:

~~a)~~ preparing a nucleic acid comprising labeled nucleotides~~;~~

~~b) sequentially removing nucleotides from one end of the nucleic acid;~~

~~c) moving the nucleotides in a stream packed with nanoparticles;~~

~~d) identifying the nucleotides by Raman spectroscopy; and~~

~~e) determining the sequence of the nucleic acid~~.

163. (Cancelled)

164. (Previously Presented) The method of claim 189, wherein each type of nucleotide is labeled with a distinguishable Raman label.

165-171. (Cancelled)

172. (Currently Amended) The method of claim ~~13~~ 188, wherein each type of nucleotide produces a unique Raman signal.

173-178 (Cancelled)

179. (Currently Amended) ~~A~~ The method of claim 188, further comprising:

~~a) removing one or more nucleotides from a nucleic acid;~~

~~b)~~ attaching each of the one or more nucleotides to at least one nanoparticle~~;~~

~~c) identifying said nucleotides; and~~

~~d) determining the sequence of said nucleic acid~~.

180. (Currently Amended) The method of claim 179, wherein said at least one nanoparticles comprises a modified surface.

181. (Cancelled)

182. (Previously Presented) The method of claim 179, wherein said nanoparticles comprise gold and/or silver.

183. (Previously Presented) The method of claim 179, wherein each nucleotide is attached to a single nanoparticle or a nanoparticle aggregate.

184-186. (Cancelled)

187. (Previously Presented) The method of claim 179, wherein said nanoparticles are between 10 nm and 20 micrometers in diameter.

188. (Previously Presented) A method comprising:

a) removing one or more nucleotides from a nucleic acid;

b) identifying each of the one or more nucleotides by Raman spectroscopy; and

c) determining the sequence of the nucleic acid.

189. (Previously Presented) The method of claim 188, wherein each type of nucleotide is labeled with a Raman label.

190. (Currently Amended) The method of claim 188, ~~comprising labeling~~ wherein the nucleic acid comprises labeled thymine.

191. (Currently Amended) The method of claim 188, ~~comprising labeling~~ wherein the nucleic acid comprises labeled adenine.

192. (Currently Amended) The method of claim 188, ~~comprising labeling~~ wherein the nucleic acid comprises labeled cytosine.

193. (Currently Amended) The method of claim 188, ~~comprising labeling~~ wherein the nucleic acid comprises labeled guanine.

194. (Currently Amended) The method of claim 188, ~~comprising labeling~~ wherein the nucleic acid comprises labeled uracil.

195. (Previously Presented) The method of claim 188, wherein said nucleotides are identified by surface enhanced Raman spectroscopy (SERS) and/or surface enhanced resonance Raman spectroscopy (SERRS).

196. (New) The method of claim 179, wherein the act of attaching each of the one or more nucleotides to at least one nanoparticle occurs prior to the act of removing one or more nucleotides from a nucleic acid.

197. (New) The method of claim 179, wherein the act of attaching each of the one or more nucleotides to at least one nanoparticle occurs after the act of removing one or more nucleotides from a nucleic acid.

198. (New) The method of claim 188, wherein the one or more nucleotides is free of an emission-enhancing aid.